

AMENDMENTS TO THE CLAIMS

1-2. (Canceled)

3. (Previously presented) The composition of Claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is a protein, peptide, nucleotide, oligonucleotide, saccharide, polysaccharide, organic molecule, or combination thereof.

4. (Previously presented) The composition of Claim 36, wherein the hydrophobic component is a synthetic vinyl hydrophobic polymer, a naturally derived polymer, a membrane disruptive peptide, or a phospholipid bilayer disrupting agent.

5-7. (Canceled)

8. (Previously presented) The composition of Claim 36, wherein the pH-sensitive linkage is an acetal, orthoester, cis-aconityl group, hydrazone, ester, Schiff base, dithioacetal, tert butyl ester, carbamate, thioester, or phosphoramidate.

9. (Previously presented) The composition of Claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is coupled to either the hydrophilic or the hydrophobic component by a degradable or disruptable linkage.

10-12. (Canceled)

13. (Previously presented) The composition of Claim 36, wherein the conjugate further comprises a ligand, wherein the ligand specifically binds to a target molecule.

14. (Previously presented) The composition of Claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is complexed to a component of the conjugate.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS^{PLLC}
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

15. (Previously presented) The composition of Claim 36, wherein the pH sensitive linkage is hydrolyzed within about 30 to 60 minutes at a pH between 5.0 and 5.5.

16. (Previously presented) The composition of Claim 36 further comprising a pharmaceutically acceptable carrier for delivery of the conjugate to a cell or organelle.

17. (Previously presented) The composition of Claim 16, wherein the carrier provides for systemic delivery of the conjugate, local delivery of the conjugate, or topical delivery of the conjugate.

18. (Canceled)

19. (Previously presented) The composition of Claim 34, wherein the therapeutic, diagnostic, or prophylactic agent is an antisense nucleotide, ribozyme, ribozyme guide sequence, triplex forming oligonucleotide, or gene.

20-33. (Canceled)

34. (Previously presented) The composition of Claim 36 further comprising an agent, wherein the agent is a therapeutic, diagnostic, or prophylactic agent.

35. (Previously presented) The composition of Claim 36, wherein the hydrophobic component comprises a synthetic polymer.

36. (Currently amended) A composition for enhancing transport through a membrane, comprising a water-soluble hydrophilic conjugate having a hydrophobic component linked to a hydrophilic component by a pH-sensitive linkage, wherein the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic

component, wherein the hydrophilic component comprises a polyalkylene oxide, wherein the hydrophobic component is a vinyl polymer, and wherein the hydrophobic component is endosomal membrane disruptive and allows enhanced transport through a membrane when released from the hydrophilic conjugate.

37. (Canceled)

38. (Previously presented) A water-soluble conjugate, comprising:

- (a) a hydrophobic synthetic vinyl polymer, wherein the polymer is endosomal membrane disruptive when released from the hydrophilic conjugate;
- (b) a plurality of pendant hydrophilic polyalkylene oxide components; and
- (c) a plurality of pH-sensitive linkages, wherein each of the pendant polyalkylene oxide components is covalently linked to the polymer through a pH-sensitive linkage that is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5.

39. (Previously presented) The conjugate of Claim 38, wherein the synthetic vinyl polymer is a terpolymer of dimethylaminoethyl methacrylate, butyl methacrylate, and styrene benzaldehyde.

40. (Previously presented) The conjugate of Claim 38, wherein the pH-sensitive linkage is selected from the group consisting of an acetal, a dithioacetal, an ester, an orthoester, and a carbamate.

41. (Previously presented) A composition, comprising:

- (a) a water-soluble hydrophilic conjugate comprising:
 - (i) a hydrophobic synthetic vinyl polymer, wherein the polymer is endosomal membrane disruptive when released from the hydrophilic conjugate;

(ii) a plurality of pendant hydrophilic polyalkylene oxide components;
and

(iii) a plurality of pH-sensitive linkages, wherein each of the pendant polyalkylene oxide components is covalently linked to the polymer through a pH-sensitive linkage that is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5; and

(b) a therapeutic or diagnostic agent.

42. (Previously presented) The composition of Claim 41, wherein the synthetic vinyl polymer is a terpolymer of dimethylaminoethyl methacrylate, butyl methacrylate, and styrene benzaldehyde.

43. (Previously presented) The composition of Claim 41, wherein the pH-sensitive linkage is selected from the group consisting of an acetal, a dithioacetal, an ester, an orthoester, and a carbamate.

44. (Previously presented) The composition of Claim 41, wherein the therapeutic or diagnostic agent is selected from the group consisting of a protein, a peptide, a saccharide, a polysaccharide, an organic molecule, a nucleotide, an antisense nucleotide, an oligonucleotide, a ribozyme, a ribozyme guide sequence, a triplex forming oligonucleotide, and a gene.

45. (Previously presented) The composition of Claim 36, wherein the hydrophobic component comprises a random, block, or graft copolymer, wherein the copolymer comprises an alkyl substituted or unsubstituted acrylate group.

46. (Previously presented) The composition of Claim 36, wherein the hydrophobic component comprises poly(ethylacrylic acid), poly(propylacrylic acid), poly(butylacrylic acid), or acrylic acid polymer and copolymers.

47. (Currently amended) A composition for enhancing transport through a membrane, comprising a hydrophilic conjugate having a hydrophobic component linked to a hydrophilic component by a pH-sensitive linkage,

wherein the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component;

wherein the hydrophilic component comprises a polyalkylene oxide;

wherein the hydrophobic component comprises a random, block, or graft copolymer, wherein the copolymer comprises an alkyl substituted or unsubstituted acrylate group; and wherein the hydrophobic component is endosomal membrane disruptive and allows enhanced transport through a membrane when released from the hydrophilic conjugate.